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10/626,301	07/23/2003	T. William Hutchens	016866-002220US	1861

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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 02/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/626,301	HUTCHENS ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2006 and 31 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27,36-38 and 40-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27, 36-38 and 40-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 27, 36-38 and 40-44 are pending and under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 27, 36-38 and 40-44, as amended, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention and reiterated below.

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the genus of the invention.

The specification, at the time of filing, does not describe a method for detecting translation of mRNA from the produced polypeptide. There is no correlation as to the polypeptide obtained to the translation of the mRNA. The specification

provides in general terms the different embodiments of the invention. At paragraph bridging pages 13 and 14, the specification states that another aspect of the invention provides a method for detecting translation of a polynucleotide. One method comprises the steps of: a) providing a substrate comprising an adsorbent for use in desorption spectrometry; b) contacting the substrate with the polynucleotide encoding a polypeptide and with agent B for in vitro translation of the polynucleotide whereby the polypeptide is produced; c) exposing the substrate to an eluant to allow retention of the polypeptide by the adsorbent; and d) detecting retained polypeptide by desorption spectrometry. Detection of the polypeptide provides detection of translation of the polynucleotide. The general aspects of the invention do not correlate to a specific description of a single species of each of the different compounds and/or reagents. The encoding polynucleotide, the polypeptide, adsorbent and /or the reagent use in the method cover such huge scope. It is well known in the art that because of the degeneracy of the genetic code, one cannot predict whether a polypeptide is the desired product that is derived from a polynucleotide translation. Other factors such as fragmentation of the polypeptide, the presence of impurities or interfering substances can affect the method. In

biotechnological invention one cannot necessarily make a priori statement without the benefit of experimental studies. There may be unpredictability in the results obtained for one species, let alone, from a genus as broadly claimed. Adequate disclosure, like enablement, requires representative examples, which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that applicant had possession of the full scope of the claimed invention. See In re Riat (CCPA 1964) 327 F2d 685, 140 USPQ 471; In re Barr. (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and University of California v. Eli Lilly and Co. (for disclosure). An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as structures, figures, diagrams, and formulas that fully set forth the claimed invention. Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir.1997). There is not a single structure for any or all of the compounds encompassed in the broad scope of the claimed method.

Response to Arguments

Applicants argue that the specification describes the presently claimed methods for detecting translation of an mRNA,

for example on page 13, line 31 through page 14,line 5 and page 70, line 28 up to page 71, line 26 and page 71, lines 13-26. It is argued that because the methods are directed to detecting the translation of an mRNA, which does not contain introns, there is a direct correlation between the nucleotide sequence of the mRNA and the translated sequence of the polypeptide.

In response, a review of page 13 up to page 14 describes a polynucleotide, not mRNA. Page 70 up to page 71 describes a differentially expressed mRNAs that has been identified by routine methods. Thus, the specification describes the identification of a polypeptide specifically antibody from the expressed mRNAs that has already been identified. A review of all the Examples that provides the detail description does not recite a single mRNA translation, let alone any type of polypeptide, except antibody.

Applicants acknowledge the degeneracy of the genetic code. But argue that even with the degeneracy of the genetic code, the specific amino acids encoded by a particular codon in an mRNA sequence have long been known in the art. The present method only requires detecting the polypeptide as an indicator of translation of the mRNA, and do not require determining or knowing the sequence of either the mRNA or the polypeptide.

In reply, it is not the sequence of the detected polypeptide that is required but a description of the mRNA from the translated polypeptide. Except for the general statement in the specification, including that the expressed mRNA has been identified for translation of a polypeptide, the specification does not described the polypeptide as providing detection of a translated mRNA.

Applicants argue that there is no evidence provided by the Office why persons skilled in the art would not recognize that the inventors had possession of the claimed invention at the time of filing.

In response, applicants' acknowledgment of the degeneracy of the codon that can result in any type of polypeptide suffices as evidence. One skilled would not correlate the single antibody polypeptide to any polypeptide let alone, to a(ny) translated mRNA.

Claims 27, 36-38 and 40-44, as amended, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention and repeated below.

The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include:

(1) the breadth of the claims,
(2) the nature of the invention,
(3) the state of the prior art,
(4) the level of one of ordinary skill;
(5) the level of predictability in the art,
(6) the amount of direction provided by the inventor,
(7) the existence of working examples, and
(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.
In re Wands, (U.S.P.Q. 2d 1400 (CAFC 1988).

1). The specification fails to give adequate direction and guidance in how to readily go about determining which polynucleotide translates into a polypeptide in situ on an adsorbent. It does not teach with specificity the detection of the polynucleotide from the polypeptide produced from the translation. It does not enable how a translation of a polynucleotide in situ in an adsorbent can be accomplished. It does not describe the kind of translation polynucleotide and/or polypeptide, adsorbent and reagents employ in the method.

2). The specification failed to provide a single working example for the translation of a polynucleotide and detection of the polypeptide presumably obtained from the translation by the polynucleotide. There are just too many and different

combinations of the compounds and reagents use in the method as well as other undefined variables.

3). The breadth of the claims encompasses a large diversity of translation polynucleotide, polypeptide, adsorbents and reagents. It is well known in the art that the diversity of the inserts in a vector as the claimed bacteriophage or host is not easily estimated. It may be for example, that only a small subset of possible peptide sequences are presented efficiently by a particular expression system. And, it is not always easy to follow the expression of peptides in particular cells; for example, to know whether or not a specific cell is expressing a member of the insert, especially for biological methods.

4). The state of the prior art is such that techniques or methods are specifically applied or adapted for a known or defined structure of a translation polynucleotide and its specifically expressed product.

5). The art is inherently unpredictable because it is not possible to predict that even with a predetermined translation polynucleotide the one that would specifically translates to a desired polypeptide. Whether the polypeptide produced is adsorbed in a certain type of adsorbent or the polypeptide correlates to the polynucleotide from which it is translated. It is generally known that there are still no rules that have

emerged that allow the translation of a polynucleotide to be related to sequence in any simple fashion (even as applied to the actual compounds).

6). Because the art is unpredictable, applicants' specification reasonably would not have assured persons skilled in the art to the numerous undefined variables of the claimed method. Applicants do not adequately enable persons skilled in the art to readily determine such. Applicants need not guarantee the success of the full scope of the claimed invention. However, skilled artisans are provided with little assurance of success.

Response to Arguments

Applicants argue that the presently claimed methods detect translation of an mRNA by detecting a translated polypeptide retained on an adsorbent. Applicants rely on e.g., page 71, line 28 through page 77, line 13.

In reply, see the response above.

Applicants argue that protocols for carrying out in vitro translation and reagents for in vitro translation were well known in the art at the time of filing of the present application. The reagents for in vitro translation were readily available in kits. Applicants attached Exhibits D-F disclosing the use of kits for practicing in vitro translation.

In response, the translation is not carried out in a substrate, as claimed. While translation of mRNA in vitro is known in the art, however, such translation is not in the context as claimed. The claim recites what appears to be in vitro translation in a substrate that is used for desorption spectrometry. The specification does not disclose any type of mRNA that translates into any kind of polypeptide and vice versa.

Applicants argue that the present methods set forth the step of providing an mRNA, which can, but need not involve the use of an expression system.

In response, the specification does not define the step of "providing". Thus, it is not clear from the specification as to this step.

Applicants submit that the operability of the present methods can be ascertained from the inventor's Yip declaration under 37 CFR 132. The declaration is alleged to states that the methods can be predictably and successfully carried out without undue experimentation.

In reply, the Yip declaration is not signed, thus is given no weight. The declaration of Lomas submitted on 10/31/2004 has also been provided. The Lomas declaration states at page 3, item 10, that the example attached to the declaration differs from

the pending claims of the present application in that in the example the protein is translated in an E.oli cell as opposed to in vitro translation recited in the claims. The declarant states that protocols for in vitro translation were well known and commonly practiced at the time of the priority date of the present application. Kits can be purchased from e.g., Promega.

In response, in order to be given weight, the declaration has to demonstrate the present claimed method. While kits are purchasable however, the specification does not teach the kits as used in the instant method. The declaration seems to affirm the expressed uncertainty as stated in the last Office action. That is the mRNA direct translation in vitro in a substrate for use for desorption spectrometry analysis. Furthermore, Exhibit B does not relate to in vitro translation on a substrate and in situ translation on the substrate. Exhibit C provides only a list of the in vitro translation of mRNA for specific polypeptide and not as applied in the instant method. Likewise, Exhibits D-F relate to a specific peptide translated from mRNA and not an in situ translation in a substrate for desorption spectrometry to detect the polypeptide as a means of translation of mRNA. [It is of interest to note that claimed clause "whereby detection of the polypeptide provides detection of translation

of the mRNA" is not present in the method steps as recited in the declaration.]

Claim Rejections - 35 USC § 112, second paragraph

Claims 27, 36-38 and 40-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention and reiterated below.

A). The method in step c as to translating the polynucleotide in situ on the adsorbent is unclear as to how this is done since this is not positively recited in the specification. The step is at odds with the specification e.g., paragraph bridging pages 3 and 4, above.

Response to Arguments

Applicants argue at page 71, lines 14-26 that the specification teaches how in vitro translation can be carried out in situ on an adsorbent by overlying the substrate with a cylindrical tube to create a well with the substrate at the base of the well. In the well, one places reagent for in vitro translation of the mRNA.

In response, this is however unclear as applied to a substrate for desorption spectrometry, as claimed.

Applicants have not responded to the above rejection that this step is at odds with the specification, paragraph bridging

pages 3 and 4. Thus, it is believed that applicants are acquiescing therewith.

In view of the amendments to the claims, the rejection of claim 27 under paragraph B is withdrawn. However, in view of the amendments the following rejections are applied:

1. Non-sequitur for "the polynucleotide" in claim 41. The base claim 27 has cancelled the term polynucleotide. This rejection has similar import to claim 43.

2. Claim 42 "the generic package" lacks antecedent basis of support from the base claim 27.

3. Claim 44 depends on cancelled claim 36, which then depends on cancelled claim 39.

Double Patenting

In view of the terminal disclaimer on the record, the obviousness rejection of the claims over U. S. Patent No. 6,225,047; U. S. Patent No. 5,719,060; U. S. Patent No. 6,579,719 and U. S. Patent No. 6,881,586 has been overcome.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 27, 36-38 and 40-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hutchens(WO 94/ in view of any one of the prior art Exhibits D-F newly cited by applicants.

Hutchens discloses at page 59, line 20 up to page 60, line 25 a method by which a lactoferrin antibody is affinity purified by thiolphilic adsorption and immobilized lactoferrin columns. The binding partner human lactoferrin is incubated with the lactoferrin adsorbed antibody and sheep anti-rabbit IgG covalently attached to a magnetic bead. The amount of the bound lactoferrin to the antibody complex is detected and quantified. The bead is then transferred and analyzed by laser desorption mass spectrometry. Figure 1 shows the presence of lactoferrin in the antigen-primary antibody-secondary antibody complex. Hutchens further discloses, at page 61, lines 2-25, that the affinity-purified anti-human lactoferrin is covalently bound to the tip of an activated nylon probe element and immersed in a preterm infant urine that contains a human lactoferrin and then the sample is analyzed by laser desorption mass spectrometry. See also page 26, lines 3-6 which discloses RNA can be attached

to the substrate. Hutchens does not disclose that the polypeptide that can be detected is a translation of mRNA. However, the different prior art cited by applicants of in vitro translation of mRNA to produce a polypeptide is well known in the art using the known protocols. Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use mRNA as an adsorbent for a substrate to detect it from polypeptide translation. Translation of a polypeptide would reasonably and expectedly lead to the identification of the gene.

No claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf
Primary Examiner
Art Unit 1639

Tdw
February 15, 2006